Patent Docket P0897P2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of David V. Goeddel and Mike Rothe Serial No.: 08/446,915 Filed: 22 May 1995 For: Tumor Necrosis Factor Receptor - Associated Factors	Group Art Unit: 1812 Examiner: J. Ulm **CERTIFICATE OF MAILING** I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231 on October 3, 1997 Aida A. Miclat Aida A. Miclat

PETITION TO ACCEPT PHOTOGRAPH AS DRAWING

37 CFR §1.84(b)

BOX ISSUE FEE
Assistant Commissioner of Patents
Washington, D.C. 20231

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GROUP 1800

Sir:

1. Petition is hereby made to accept a photograph in this case.

2. Three (3) copies of the photograph of Figures 1, 2a, 2b, 3, 4, 5, 6a, 6b, 7, 8, 9, 15a, 15b, 16 and 17, are submitted herewith. It is submitted that photographs are the only medium by which to disclose certain aspects of the subject matter sought to be patented in this application.

3. The petition fee under 37 CFR 1.17(h) of $130.00 is to be charged to Deposit Account No. 07-0630. Please charge any deficiency or credit any overpayment to Deposit Account No. 07-0630. A duplicate copy of this sheet is enclosed.

12/02/1997 MDEOPLES 00000026 DAH:070630 08446915
01 FC:122 130.00 CH

Respectfully submitted,

GENENTECH, INC.

Date: October 3, 1997

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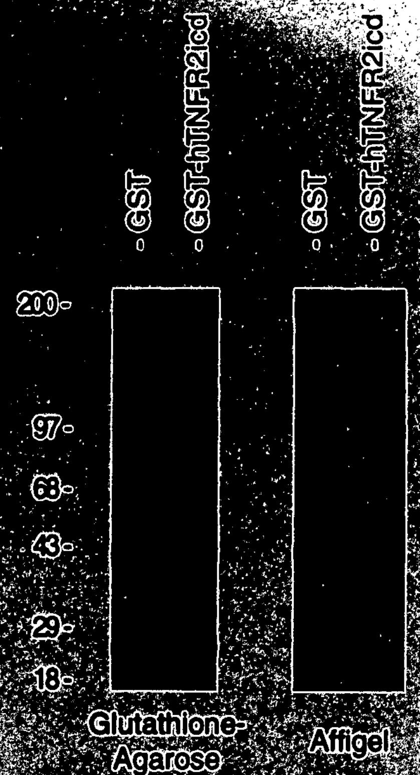
Revised (10/13/95)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GST
GST-hTNFR2icd
200-
97-
68-
43-
29-
18-
Glutathione-Agarose
Affigel

FIG. 4

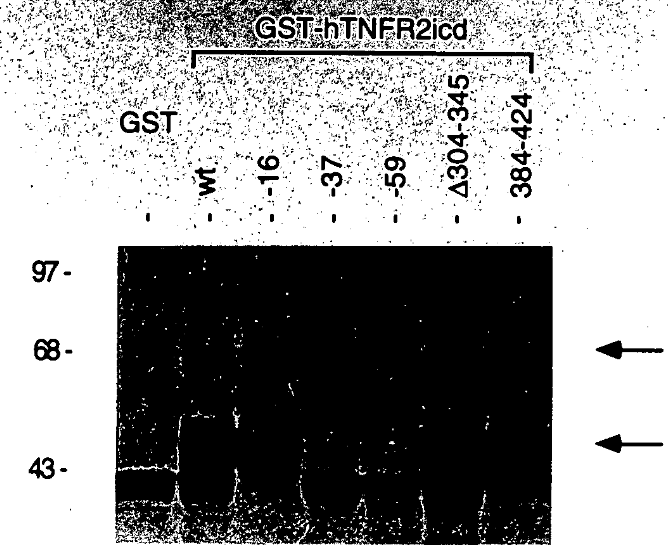
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FIG. 5

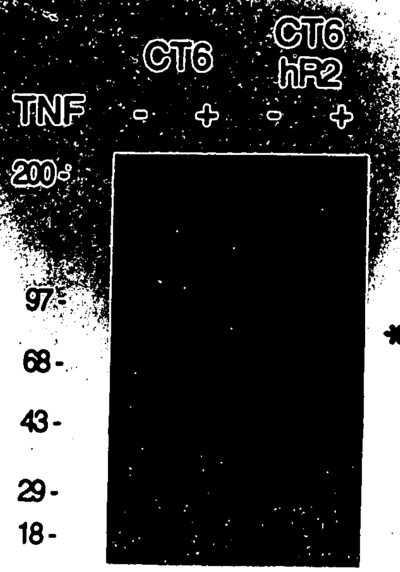
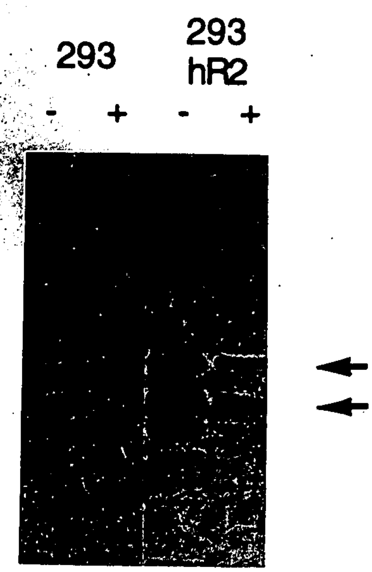


FIG. 2a



CT6

FIG. 2b

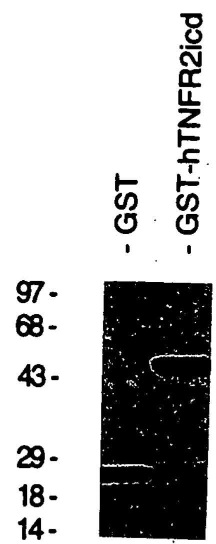


FIG. 3

5741667

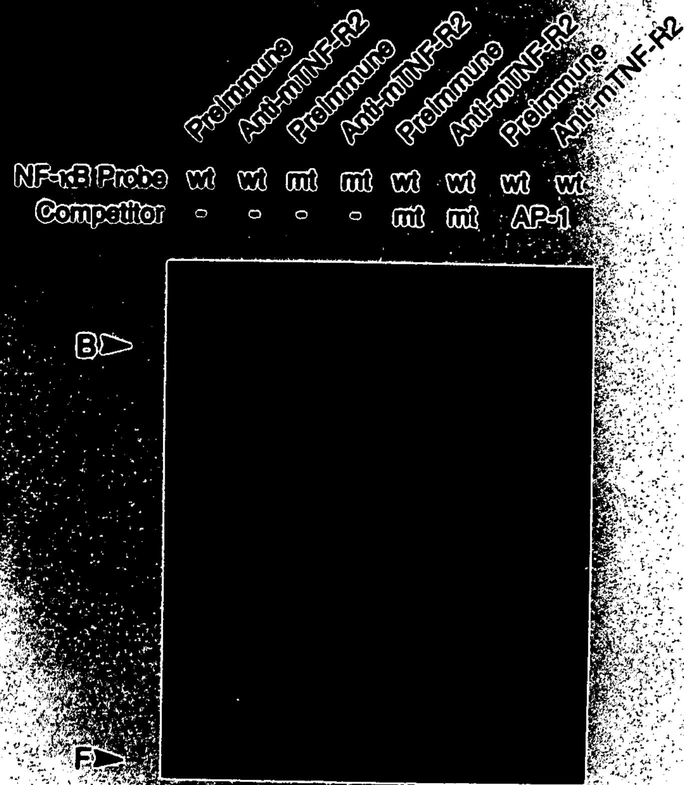


FIG. 1

FIG. 6a

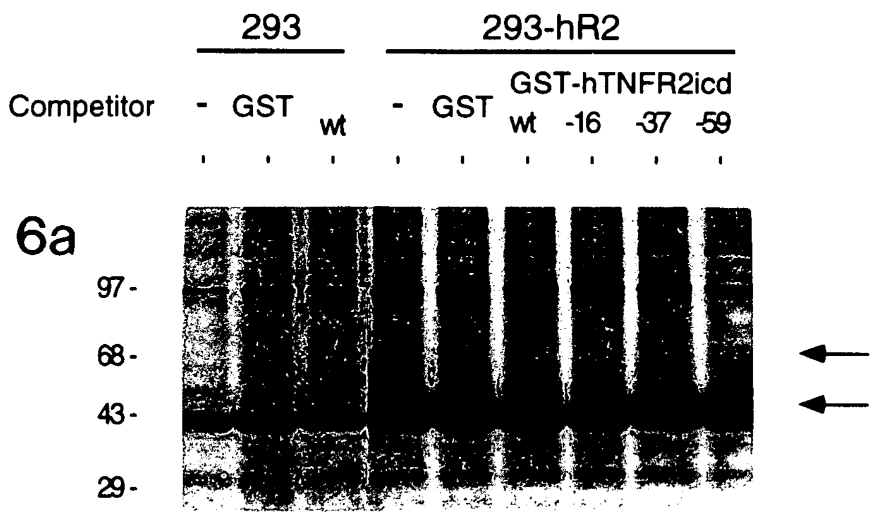


FIG. 6b

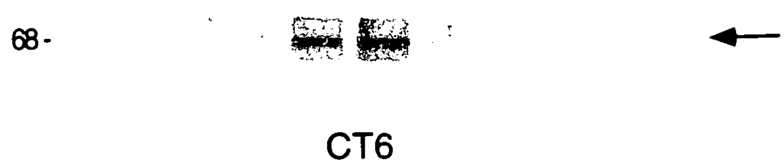
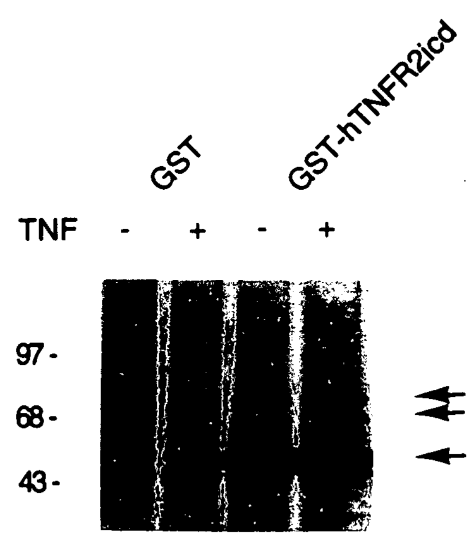


FIG. 7



APPROVED	O.G. FIG	
	CLASS	SUBCLASS
DRAFTSMAN		

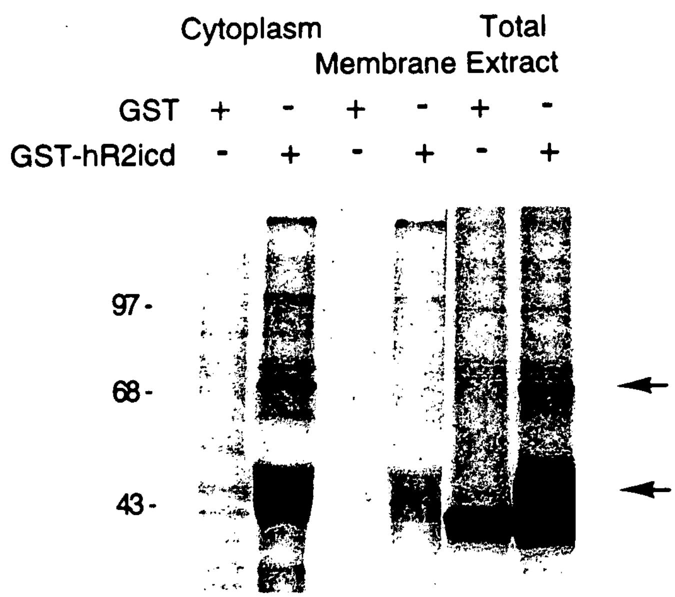


FIG. 8

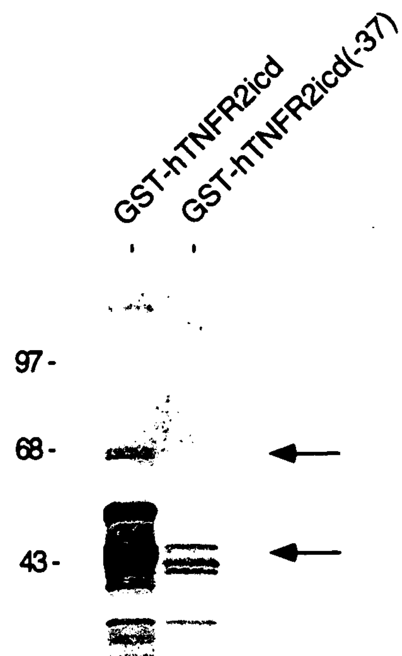


FIG. 9

1 CCCAGCCCGGTTCTCTGCCCCAAGGACGCTACCGCCCAATGCGAGCAGAAGGCGGCGCACAGATACAGAAAGT
74 GAGGCTCAGACATATTGAAGACCGTGTGACATAGGGTAGCCAAATGACAGTGTGAGAAAGTGACATTTACTCAAG
149 GCCACCCAGATATCCTGGAGGACCCAGAACCCTGGAGATTCCCATCAGAAAGACCTTCTGGCCACCTGAAACCCC

1 MetAlaSerSerSerAlaProAspGluAsnGluPheGlnPheGlyCysProProAlaProCysGlnAspPro
224 AAGATGGCCTCCAGCTCAGCCCCTGATGAAAACGAGTTTCAATTTGGTTGCCCCCCTGCTCCCTGCCAGGACCCA

25 SerGluProArgValLeuCysCysThrAlaCysLeuSerGluAsnLeuArgAspAspGluAspArgIleCysPro
299 TCGGAGCCCAGAGTTCTCTGCTGCACAGCCTGTCTCTCTGAGAACCTGAGAGATGATGAGGATCGGATCTGTCCT

50 LysCysArgAlaAspAsnLeuHisProValSerProGlySerProLeuThrGlnGluLysValHisSerAspVal
374 AAATGCAGAGCAGACAACCTCCATCCTGTGAGCCCAGGAAGCCCTCTGACTCAGGAGAAGGTTCACTCTGATGTA

75 AlaGluAlaGluIleMetCysProPheAlaGlyValGlyCysSerPheLysGlySerProGlnSerMetGlnGlu
449 GCTGAGGCTGAAATCATGTGCCCCTTTGCAGGTGTTGGCTGTTCCTTCAAGGGGAGCCCACAATCCATGCAGGAG

100 HisGluAlaThrSerGlnSerSerHisLeuTyrLeuLeuLeuAlaValLeuLysGluTrpLysSerSer**ProGly**
524 CATGAGGCTACCTCCCAGTCCTCCCACCTGTACCTGCTGCTGGCGGTCTTAAAGGAGTGGAAATCCTCACCAGGC

125 **SerAsnLeuGlySerAlaProMetAlaLeuGluArg**AsnLeuSerGluLeuGlnLeuGlnAlaAlaValGluAla
599 TCCAACCTAGGGTCTGCACCCATGGCACTGGAGCGGAACCTGTCAGAGCTGCAGCTTCAGGCAGCTGTGGAAGCG

150 ThrGlyAspLeuGluValAspCysTyrArgAlaProCysCysGluSerGlnGluGluLeuAlaLeuGlnHisLeu
674 ACAGGGGACCTGGAGGTAGACTGCTACCGGGCACCTTGCTGTGAGAGCCAGGAAGAACTGGCCCTGCAGCACTTG

175 ValLysGluLysLeuLeuAlaGlnLeuGluGluLysLeuArgValPheAlaAsnIleValAlaValLeuAsnLys
749 GTGAAGGAGAAGCTGCTGGCTCAGCTGGAGGAGAAGCTGCGTGTGTTTGCAAACATTGTTGCTGTCCTCAACAAG

200 GluValGluAlaSerHisLeuAlaLeuAlaAlaSerIleHisGlnSerGlnLeuAspArgGluHisLeuLeuSer
824 GAAGTGGAGGCTTCCCACCTGGCACTGGCCGCCTCCATCCACCAGAGCCAGTTGGACCGAGAGCACCTCCTGAGC

225 LeuGluGlnArgValValGluLeuGlnGlnThrLeuAlaGlnLysAspGlnValLeuGlyLysLeuGluHisSer
899 TTGGAGCAGAGGGTGGTGGAATTACAGCAAACCCTGGCTCAAAAAGACCAGGTCCTGGGCAAGCTTGAGCACAGT

FIG. 10a

```
250 LeuArgLeuMetGluGluAlaSerPheAspGlyThrPheLeuTrpLysIleThrAsnValThrLysArgCysHis
974 CTGCGACTCATGGAGGAGGCATCCTTTGATGGTACTTTCCTGTGGAAGATCACCAATGTCACCAAGCGGTGCCAC

275 GluSerValCysGlyArgThrValSerLeuPheSerProAlaPheTyrThrAlaLysTyrGlyTyrLysLeuCys
1049 GAGTCAGTGTGTGGCCGGACTGTCAGCCTCTTCTCTCCAGCTTTCTACACTGCCAAGTATGGTTACAAGTTGTGC

300 LeuArgLeuTyrLeuAsnGlyAspGlySerGlyLysLysThrHisLeuSerLeuPheIleValIleMetArgGly
1124 CTGCGCTTGTACCTGAACGGGGATGGCTCAGGCAAGAAGACCCACCTGTCCCTCTTCATCGTGATCATGAGAGGA

325 GluTyrAspAlaLeuLeuProTrpProPheArgAsnLysValThrPheMetLeuLeuAspGlnAsnAsnArgGlu
1199 GAATACGATGCTCTCCTGCCCTGGCCTTTCAGGAACAAGGTCACCTTTATGCTACTTGACCAGAACAACCGAGAG

350 HisAlaIleAspAlaPheArgProAspLeuSerSerAlaSerPheGlnArgProGlnSerGluThrAsnValAla
1274 CATGCTATTGATGCCTTCCGGCCTGACCTGAGCTCAGCCTCCTTCCAGCGGCCACAGAGTGAGACCAACGTGGCC

375 SerGlyCysProLeuPhePheProLeuSerLysLeuGlnSerProLysHisAlaTyrValLysAspAspThrMet
1349 AGCGGCTGCCCGCTCTTCTTCCCCCTCAGCAAGCTGCAGTCACCCAAGCACGCCTACGTCAAAGATGACACAATG

                                              <
400 PheLeuLysCysIleValAspThrSerAla
1424 TTCCTCAAATGCATTGTGGACACTAGTGCTTAGGGATGGGGGGAGGGGGTGTCTCCTGACAGAACCAGCTTAGAC
1499 TGGGGGACTTAGCTAGACAGCCAGGCCCTGCCTGCCCTTGGAGCCCACAGCCCACGACAAGGAGGAGCCAAGGCT
1574 GGCATGACTTCAGCGCCACAGCATGCTGGTTATGGCTGATGTGAGGCTGGAGAAACGTGTGCGTACAGAGACAGA
1649 GTGGAGGAGAAGACAGAAGTGCTCTTTTCACACAGACTACACGACACCAGGAGGCCAGCATGCCAGCAGCTTCTG
1724 AATGTTGAGACCAGCCTAGATCAGGATGAAAAGAGCCAGGCCTGAGGCTTGGACATTGAGCCAAGGCTATGGGGC
1799 CTAAGTGGAGGGGCACTCCTACCAGGACATTCTCTCGAGGTCAGGGCATAACTGGAAAAATGCCCCCATCTCTCT
1874 GTTCAGACTCAAAACTAGAACCACAGGGCAGAAGGGTCAGACATTAATGTGAATTTAACCTGCCCTGGACTGAGT
1949 TCCTATGTTAACAGACACGCAAACAGGTAAACCCAGAAACTGCCCTGGGAAATGCTTTCTGGCTGCATCTGGAGA
2024 TCTTTGATGTTTTTACCGACAAAACAAATAACAAAAGCCTTGAATTGCAAAAAAAAAAAAAAAAA
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FIG. 10b

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

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        ^*   *          *   *
  1                                                  MetAlaAlaAlaSerValThrSerPro
  1   GCGCGAAGACCGTTGGGGCTTTGTGGTGTGTGGGGGTTGTAACTCACATGGCTGCAGCCAGTGTGACTTCCCCT

 10  GlySerLeuGluLeuLeuGlnProGlyPheSerLysThrLeuLeuGlyThrArgLeuGluAlaLysTyrLeuCys
 75  GGCTCCCTAGAACTGCTACAGCCTGGCTTCTCCAAGACCCTCCTGGGGACCAGGTTAGAAGCCAAGTACCTCTGT

 35  SerAlaCysLysAsnIleLeuArgArgProPheGlnAlaGlnCysGlyHisArgTyrCysSerPheCysLeuThr
150  TCAGCCTGCAAAAACATCCTGCGGAGGCCTTTCCAGGCCCAGTGTGGGCACCGCTACTGCTCCTTCTGCCTGACC

 60  SerIleLeuSerSerGlyProGlnAsnCysAlaAlaCysValTyrGluGlyLeuTyrGluGluGlyIleSerIle
225  AGCATCCTCAGCTCTGGGCCCCAGAACTGTGCTGCCTGTGTCTATGAAGGCCTGTATGAAGAAGGCATTTCTATT

 85  LeuGluSerSerSerAlaPheProAspAsnAlaAlaArgArgGluValGluSerLeuProAlaValCysProAsn
300  TTAGAGAGTAGTTCGGCCTTTCCAGATAACGCTGCCCGCAGAGAGGTGGAGAGCCTGCCAGCTGTCTGTCCCAAT

110  AspGlyCysThrTrpLysGlyThrLeuLysGluTyrGluSerCysHisGluGlyLeuCysProPheLeuLeuThr
375  GATGGATGCACTTGGAAGGGGACCTTGAAAGAATACGAGAGCTGCCACGAAGGACTTTGCCCATTCCTGCTGACG

135  GluCysProAlaCysLysGlyLeuValArgLeuSerGluLysGluHisHisThrGluGlnGluCysProLysArg
450  GAGTGTCCTGCATGTAAAGGCCTGGTCCGCCTCAGCGAGAAGGAGCACCACACTGAGCAGGAATGCCCCAAAAGG

160  SerLeuSerCysGlnHisCysArgAlaProCysSerHisValAspLeuGluValHisTyrGluValCysProLys
525  AGCCTGAGCTGCCAGCACTGCAGAGCACCCTGTAGCCACGTGGACCTGGAGGTACACTATGAGGTCTGCCCCAAG

185  PheProLeuThrCysAspGlyCysGlyLysLysLysIleProArgGluThrPheGlnAspHisValArgAlaCys
600  TTTCCCTTAACCTGTGATGGCTGTGGCAAGAAGAAGATCCCTCGGGAGACGTTTCAGGACCATGTTAGAGCATGC

210  SerLysCysArgValLeuCysArgPheHisThrValGlyCysSerGluMetValGluThrGluAsnLeuGlnAsp
675  AGCAAATGCCGGGTTCTCTGCAGATTCCACACCGTTGGCTGTTCAGAGATGGTGGAGACTGAGAACCTGCAGGAT

235  HisGluLeuGlnArgLeuArgGluHisLeuAlaLeuLeuLeuSerSerPheLeuGluAlaGlnAlaSerProGly
750  CATGAGCTGCAGCGGCTACGGGAACACCTAGCCCTACTGCTGAGCTCATTCTTGGAGGCCCAAGCCTCTCCAGGA

                                               >          +
260  ThrLeuAsnGlnValGlyProGluLeuLeuGlnArgCysGlnIleLeuGluGlnLysIleAlaThrPheGluAsn
825  ACCTTGAACCAGGTGGGGCCAGAGCTACTCCAGCGGTGCCAGATTTTGGAGCAGAAGATAGCAACCTTTGAGAAC
```

FIG. 11a

```
285  IleValCysValLeuAsnArgGluValGluArgValAlaValThrAlaGluAlaCysSerArgGlnHisArgLeu
900  ATTGTCTGCGTCTTGAACCGTGAAGTAGAGAGGGTAGCAGTGACTGCAGAGGCTTGTAGCCGGCAGCACCGGCTA

310  AspGlnAspLysIleGluAlaLeuSerAsnLysValGlnGlnLeuGluArgSerIleGlyLeuLysAspLeuAla
975  GACCAGGACAAGATTGAGGCCCTGAGTAACAAGGTGCAACAGCTGGAGAGGAGCATCGGCCTCAAGGACCTGGCC

335  MetAlaAspLeuGluGlnLysValSerGluLeuGluValSerThrTyrAspGlyValPheIleTrpLysIleSer
1050 ATGGCTGACCTGGAGCAGAAGGTCTCCGAGTTGGAAGTATCCACCTATGATGGGGTCTTCATCTGGAAGATCTCT

360  AspPheThrArgLysArgGlnGluAlaValAlaGlyArgThrProAlaIlePheSerProAlaPheTyrThrSer
1125 GACTTCACCAGAAAGCGTCAGGAAGCCGTAGCTGGCCGGACACCAGCTATCTTCTCCCCAGCCTTCTACACAAGC

385  ArgTyrGLyTyrLysMetCysLeuArgValTyrLeuAsnGlyAspGlyThrGlyArgGlyThrHisLeuSerLeu
1200 AGATATGGCTACAAGATGTGTCTACGAGTCTACTTGAATGGCGACGGCACTGGGCGGGGAACTCATCTGTCTCTC

410  PhePheValValMetLysGlyProAsnAspAlaLeuLeuGlnTrpProPheAsnGlnLysValThrLeuMetLeu
1275 TTCTTCGTGGTGATGAAAGGCCCCAATGATGCTCTGTTGCAGTGGCCTTTTAATCAGAAGGTAACATTGATGTTG

435  LeuAspHisAsnAsnArgGluHisValIleAspAlaPheArgProAspValThrSerSerSerPheGlnArgPro
1350 CTGGACCATAACAACCGGGAGCATGTGATCGACGCATTCAGGCCCGATGTAACCTCGTCCTCCTTCCAGAGGCCT

460  ValSerAspMetAsnIleAlaSerGlyCysProLeuPheCysProValSerLysMetGluAlaLysAsnSerTyr
1425 GTCAGTGACATGAACATCGCCAGTGGCTGCCCCCTCTTCTGCCCTGTGTCCAAGATGGAGGCCAAGAATTCCTAT

485  ValArgAspAspAlaIlePheIleLysAlaIleValAspLeuThrGlyLeu
1500 GTGCGGGATGATGCGATCTTCATCAAAGCTATTGTGGACCTAACAGGACTCTAGCCACCCCTGCTAAGAATAGCA
1575 GCTCAGTGAGGAGCTGTCACATTAGGCCAGCCAGGCCCTGCCACACACGGGTGGGCAGGCTTGGTGTAAATGCTG
1650 GGGAGGGCCTCAGCCTAGAGCCAATCACCATCACACAGAAAGGCAGGAAGAAGCCTCCAGTTGGCCTTCAGCTGG
1725 CAAACTGAGTTGGACGGTCCACTGAGCTCAAGGGCCTGGTGGAGCCCGCTGGGGAGCTTCTCAGCTTTCCAATAG
1800 GAAAGCTCCTGCTGTCTCCTCTGTCTGGGGAAGGGAGAGACCTGTAGGTGGGTGCTCAGAAAGGGCCTCTCCAGA
1875 GAGAGTCTCAAGAGCTGCAGCAGGAGCAAAGTGACTGGCCTTCCCCACCCCATCCTTTGGAAAAGAGGTAGCGGC
1950 TACACAGGAGAAGGCATGCGCCTGCAGGGTGTAGCCCAAGAGAGAAGCTCTCTGAGACATAGGCCCTCACTGGAG
2025 AAGGGCCTGCCTGGGCTGCACAGCCTTGCCAGGTGGCCTGTATGGGGGAGAAGTGATTAAATGTTGAGATGTCAC
2100 ACGACAAAAAAAAAAAAAAAAA
```

FIG. 11b

FIG. 12a

TRAF2	(mouse)	31	KYLCSACKNILRRPFQA	QCGHRYCSFCLTSI	LSS	GPQNCAACVYE
COP1	(*A. thaliana*)	49	DLLCPICMQIIKDAFLT	ACGHSFCYMCIITH	LRN	KSDCPCCSQH
EFP	(human)	10	ELSCSICLEPFKEPVTT	PCGHNFCGSCLNETWA	VQG	SPYLCPQCRAV
RAD-18	(*S. cerevisiae*)	25	LLRCHICKDFLKVPVLT	PCGHTFCSLCIRTH	LNN	QPNCPLCLFE
UVS-2	(*N. crassa*)	31	AFRCHVCKDFYDSPMLT	SCNHTFCSLCIRRC	LSV DSK	CPLCRAT
RAG-1	(human)	290	SISCQICEHILADPVET	NCKHVFCRVCILRC	LKV	MGSYCPSCRYP
SS-A/Ro	(human)	13	EVTCPICLDPFVEPVSI	ECGHSFCQECISQV	GKG	GGSVCAVCRQR
RING1	(human)	16	ELMCPICLDMLKNTMTTKE	CLHRFCSDCIVTA	LRS	GNKECPTCRKK
RPT-1	(mouse)	12	EVTCPICLELLKEPVSA	DCNHSFCRACITLNYESNRNTDGKGN		CPVCRVP
RFP	(human)	13	ETTCPVCLQYFAEPMML	DCGHNICCACLARCWGTA		ETNVSCPQCRET
c-cbl	(human)	378	FQLCKICAENDKDVKIE	PCGHLMCTSCLTS	WQESEGQ	GSSGCPFCRCE

	X11-12		X10-16	
consensus	---C--C------------	C-H--C--C	----------------	C--C---

FIG. 12b

TRAF2	(mouse)	157	CPKRSLSCQHC RAPCSHVDLEVHYE VC
		182	PKFPLTCDGCGKKKIPRETFQDHVR AC
DG17	(*D. discoideum*)	171	GGFKLVTCDFCKRDDIKKKELETHYK TC
TFIIIA	(*X. laevis*)	189	QD LAVCDVCNRKFRHKDYLRDHQK TH
XLCOF14	(*X. laevis*)	1	TGKYPFICSECGKSFMDKRYLKIHSN VH
XFIN	(*X. laevis*)	1225	TGEKPYTCTVCGKKFIDRSSVVKHSR TH
ZFY1/2	(mouse)	521	RKKFPHICGECGKGFRHPSALKKHIR VH
MFG2	(mouse)	293	SEEKPFECEECGKKFRTARHLVKHQR IH
RAD18	(*S. cerevisiae*)	183	PNEQMAQCPICQQFYPLKALEKTHLD EC
UVS-2	(*N. crassa*)	182	PDDGLVACPICLTRM KEQQVDRHLDTSC

```
TRAF2    1 MAAASVTSPGSLELLQPGFSKTLLGTRLEAKYLCSACKNILRRPFQAQCG

TRAF2   51 HRYCSFCLTSILSSGPQNCAACVYEGLYEEGISILESSSAFPDNAARREV

TRAF2  101 ESLPAVCPNDGCTWKGTLKEYESCHEGLCPFLLTECPACKGLVRLSEKEH
TRAF1    1 ...............................MASSSAPDENEFQFGCPPA

TRAF2  151 HTEQECPKRSLSCQHCRAPCSHVDLEVHYEVCPKFPLTCDGCGKKKIPRE
TRAF1   20 PCQDPSEPRVLCCTACLSENLRDDEDRICPKCRADNLHPVSPG-SPLTQE

TRAF2  201 TFQDHVRACSKCRVLCRFHTVGCSEMVETENLQDHELQRLREHLALLLSS
TRAF1   69 KVHSDV---AEAEIMCPFAGVGCSFKGSPQSMQEHEATSQSSHLYLLLAV

TRAF2  251 FLEAQASPGTLNQVGPELLQR.............................
TRAF1  116 LKEWKSSPGSNLGSAPMALERNLSELQLQAAVEATGDLEVDCYRAPCCES

TRAF2  272 ..............CQILEQKIATFENIVCVLNREVERVAVTAEACSRQH
TRAF1  166 QEELALQHLVKEKLLAQLEEKLRVFANIVAVLNKEVEASHLALAASIHQS

TRAF2  308 RLDQDKIEALSNKVQQLERSIGLKDLAMADLEQKVSELEVSTYDGVFIWK
TRAF1  216 QLDREHLLSLEQRVVELQQTLAQKDQVLGKLEHSLRLMEEASFDGTFLWK

TRAF2  358 ISDFTRKRQEAVAGRTPAIFSPAFYTSRYGYKMCLRVYLNGDGTGRGTHL
TRAF1  266 ITNVTKRCHESVCGRTVSLFSPAFYTAKYGYKLCLRLYLNGDGSGKKTHL

TRAF2  408 SLFFVVMKGPNDALLQWPFNQKVTLMLLDHNNREHVIDAFRPDVTSSSFQ
TRAF1  316 SLFIVIMRGEYDALLPWPFRNKVTFMLLDQNNREHAIDAFRPDLSSASFQ

TRAF2  458 RPVSDMNIASGCPLFCPVSKME-AKNSYVRDDAIFIKAIVDLTGL
TRAF1  366 RPQSETNVASGCPLFFPLSKLQSPKHAYVKDDTMFLKCIVDTSA
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FIG. 13

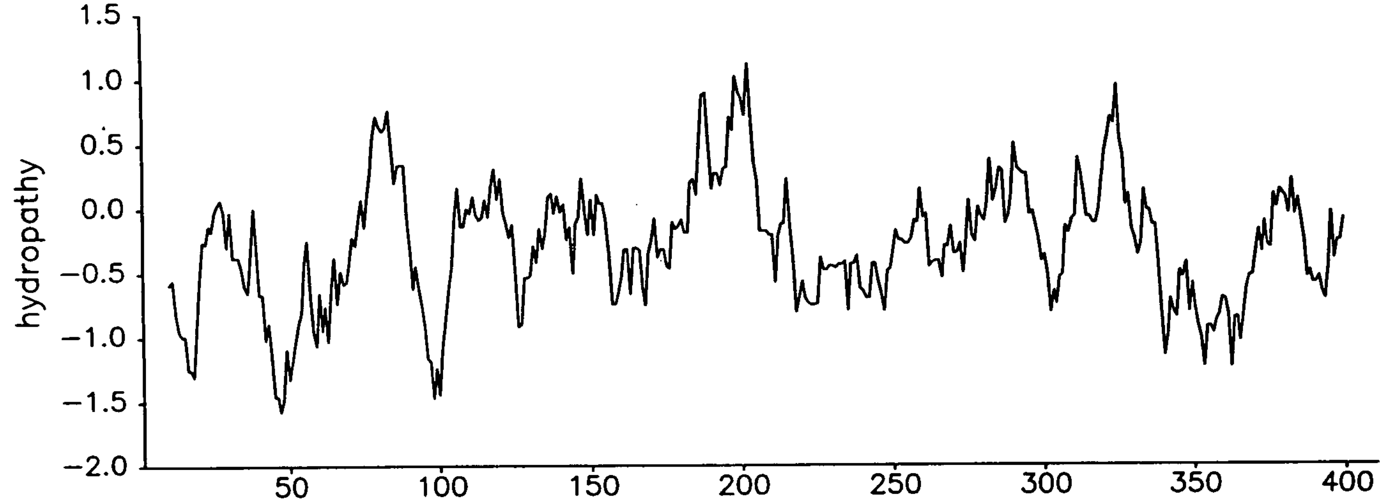


FIG. 14a

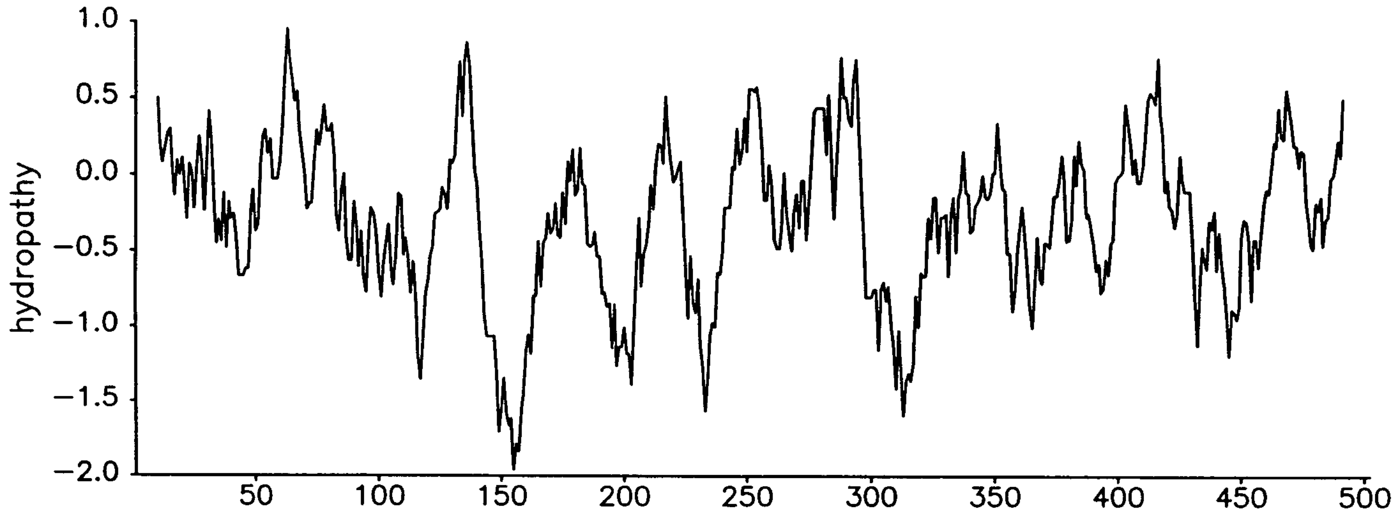

hydropathy
1.0
0.5
0.0
−0.5
−1.0
−1.5
−2.0
50
100
150
200
250
300
350
400
450
500

FIG. 14b

FIG. 18a

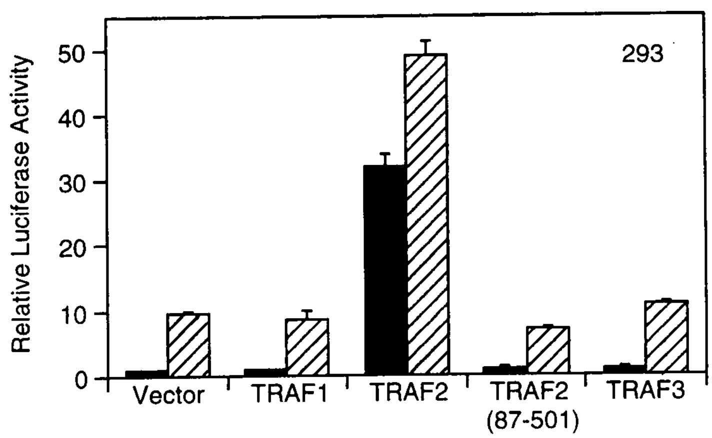


FIG. 18b

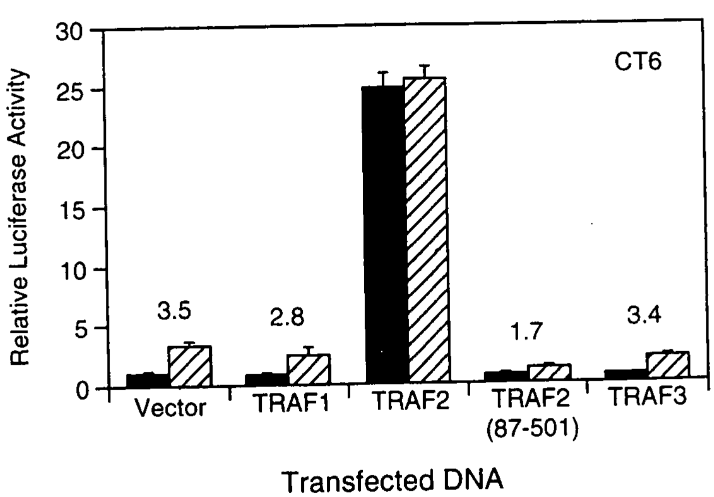


FIG. 19a

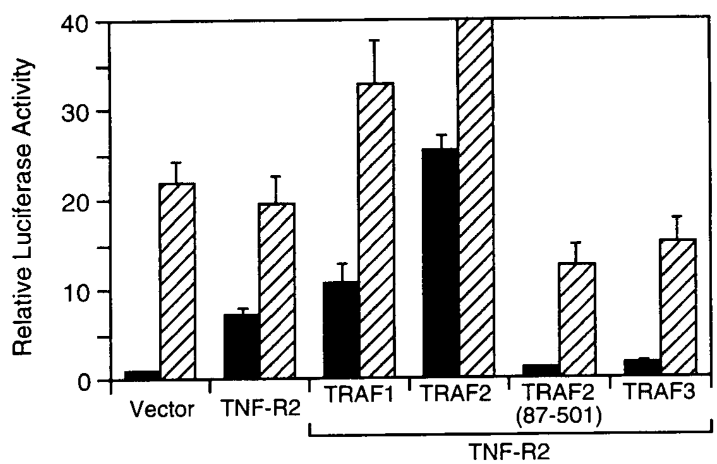
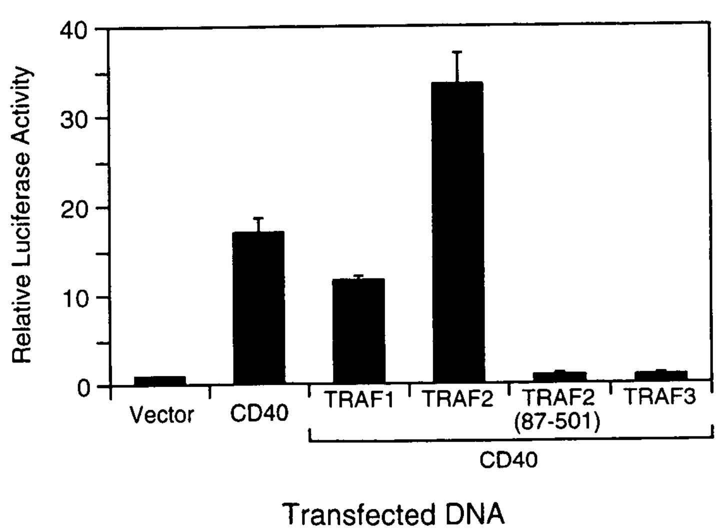


FIG. 19b



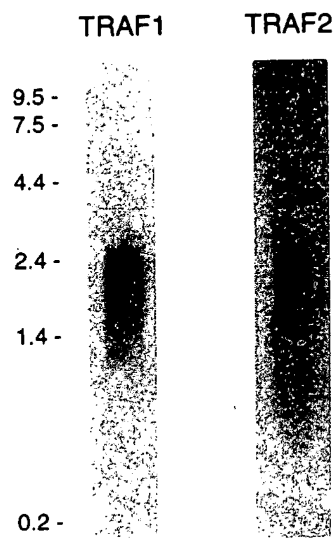


FIG. 15a

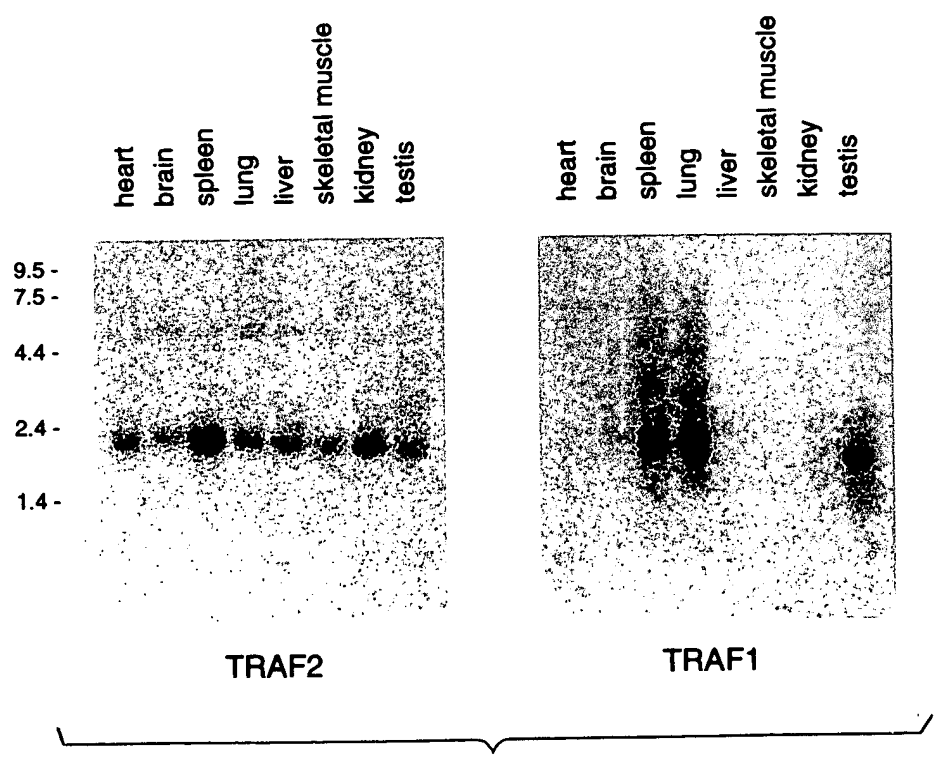


FIG. 15b

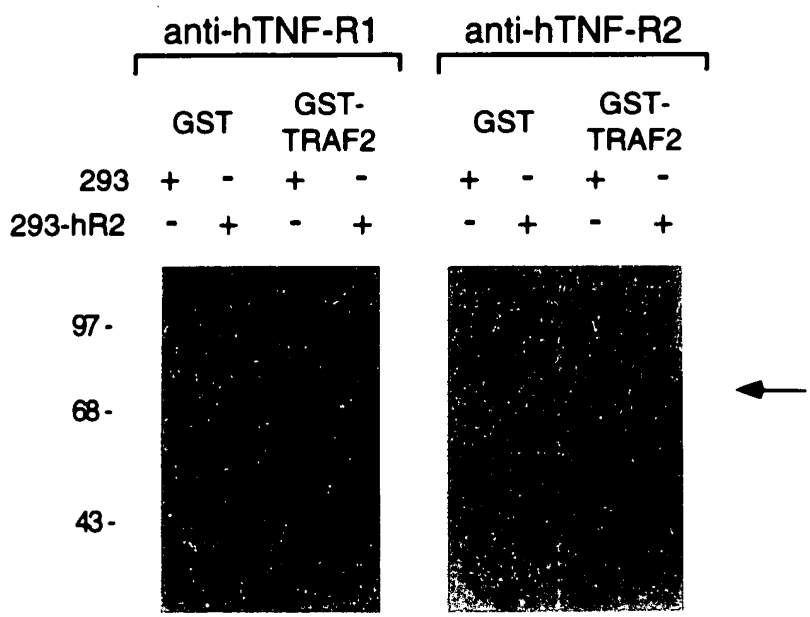
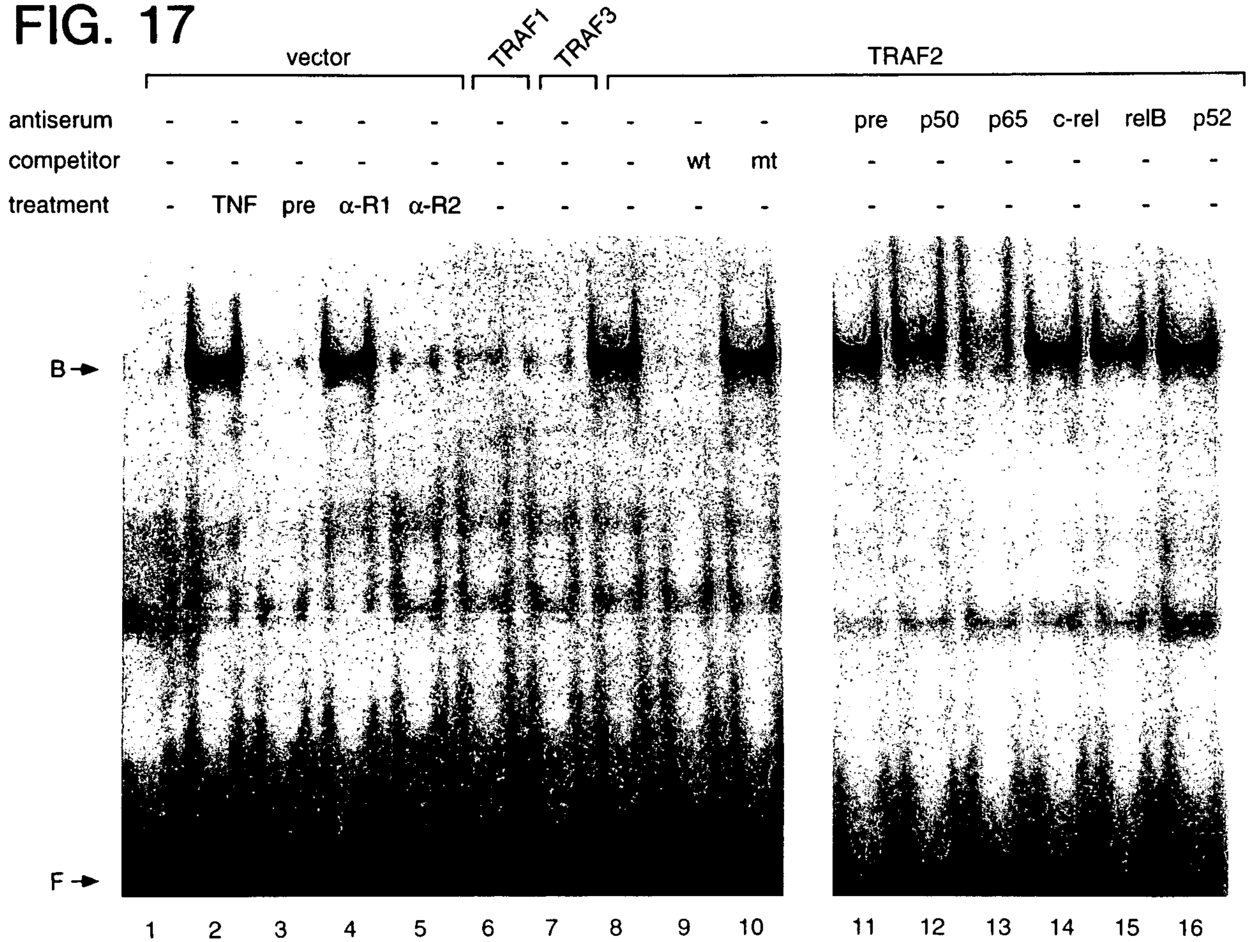

anti-hTNF-R1
anti-hTNF-R2
GST
GST-TRAF2
GST
GST-TRAF2
293 + - + - + - + -
293-hR2 - + - + - + - +
97 -
68 -
43 -

FIG. 16

FIG. 17


vector
TRAF1
TRAF3
TRAF2
antiserum - - - - - - - - - - pre p50 p65 c-rel relB p52
competitor - - - - - - - - wt mt - - - - - -
treatment - TNF pre α-R1 α-R2 - - - - - - - - - - -
B
F
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16